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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/613,903	07/11/2000	Heather J. Jordan	IVGN 187.1 CON	1446

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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
12/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/613,903	JORDAN, HEATHER J.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *141-164* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *141-164* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 October 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/08/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The use of the trademark SYBR has been noted in this application. While it has been capitalized, it also needs to be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 158 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 158 is indefinite as it incorporates a product identified by way of a registered trademark. It is noted that products identified via a trademark are subject to change without public notice. Applicant is urged to consider inserting in the claim the generic terminology (composition or formulation) represented by the trademark at the time of the invention.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 141 and 150-164 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As presently worded, the nucleic acid ladder of claims 141 and 150-164 can have virtually any upper limit a well as any lower limit, down to and including single nucleotides. A review of the disclosure fails to find support for where applicant contemplated such an invention and lesser still, an adequate written description of the invention that reasonably suggest that applicant had possession of such embodiments at the time of the invention.

7. In support of this position, attention is directed to page 4, last paragraph, bridging to page 5, first full paragraph. As stated therein the ladder can range from 10 bp (page 4, last line bridging to page 5, line 2) to "about 25 kb" (page 5, line 9).

Claim Rejections - 35 USC § 102/103

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 141-157 and 159-164 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over either US Patent 5,316,908 (Carlson et al.) or Stratagene (1993) or Stratagene Catalog (1993).

13. For purposes of examination, the claims have been construed as encompassing not only those fragments that have "substantially equivalent" relative mass, but may also include additional nucleic acid fragments that do not have "substantially equivalent" relative mass. Support for this interpretation is based on the inclusion of the term "comprising" in the sole independent claim, claim 141.

14. Said claims have also been construed as encompassing nucleic acid fragments that manifest as "discrete bands of substantially equal intensity...when the fragments are resolved on a gel and stained" (specification at page 6, first full paragraph).

15. The aspect of what constitutes the metes and bounds of "substantially equivalent" relative mass and intensity has been construed as allowing for a 3-fold increase and/or decrease over a set value. Accordingly, such language has been construed as allowing for a 6-fold range in relative mass and/or signal intensity. Support for this interpretation is found at page 9 of the specification which states in part: "Relative mass is substantially equal when the relative mass of each fragment is no more than 3 times the relative mass of another fragment..."

16. Carlson et al., Fig. 1, disclose a nucleic acid ladder that meets a limitation of claims 141-157 and 159-164.

17. It is noted with particularity that a compound and its properties are inseparable. While one may identify new properties or new means for evaluating same, such does not make an old compound, or old composition, new and patentable. The clams recite no chemical or physical component that would make the nucleic acid of the claims any different from the nucleic acid ladders of the prior art. Indeed, page 8, fifth paragraph, of the specification states in part: "However, any nucleic acid molecule or combination of molecules may be used to produce the ladders or compositions of he invention."

18. While Fig. 1 is a drawing and not a photograph, the specification does state that the Figure does represent the migration of the nucleic acid ladder in an electrophoretic environment. Said Figure clearly shows that the bands have the same relative intensity.

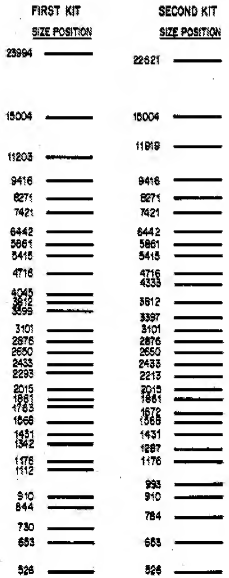


FIG.1

19. To the extent that claim 159 does positively recite that the ladder is stained with ethidium bromide, it is noted that Carlson et al. disclose such, at column 4. For purposes of examination, ethidium bromide is construed to meet the requirements of a dye as it is typically used to stain the entire gel, and with it, stain (dye) preferentially the nucleic acids therein. Accordingly, a limitation of claims 157, 159, and 160 are deemed to be met by the disclosure of Carlson et al.

20. Carlson et al., disclose nucleic acid ladders that comprise numerous bands that span a wide range of fragment sizes. While some of the rungs of the nucleic acid ladder fall within the recited ranges of claims 142-149, the disclosed nucleic acid ladders also comprise additional nucleic acid fragments that are outside of the recited range. Such additional bands do not detract from the instant rejection as the claims, through the use of the term "comprising" (claim 141, line 1) allows for the inclusion of additional reagents (rungs of a ladder), even in significant amounts.

21. The claims do not recite any material difference in the composition of nucleic acid individual fragments. Further, there is no specific wording as to the copy number of the fragments of any given size, or combination of sizes.

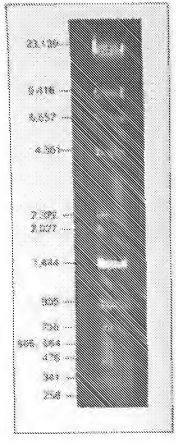
22. While newly presented claims have language directing to how the relative mass is to be calculated, it is noted that the instant claims are drawn to a composition, not to a method. Accordingly, the same composition, defined by other terms, can and does anticipate the claimed invention. In support of this position, attention is directed to page 6 of the disclosure which states in part:

> Preferably, the relative mass of each different sized fragment is substantially equivalent such that discrete bands of substantially equal intensity are produced when the fragments are resolved on a gel and stained.

23. Stratagene, at page T22, disclose a Lambda/Hind III nucleic acid ladder. As seen in the image, the ladder comprises multiple fragments that appear to have "substantially equal intensity." The ladder clearly comprises at least two fragments larger than 1 kb and two fragments less than 1 kb which have "substantially equal intensity." Given that a compound and its properties are inseparable, and given applicants statement that nucleic acid fragments that

have "substantially equivalent intensities" also have substantially equivalent relative mass (*supra*), the fragments of Stratagene are deemed to anticipate the claimed nucleic acid ladder.

24. To the degree that claims 142-156 define alternative ranges of the fragment sizes, the nucleic acid fragments of Stratagene clearly fall within each of the stated ranges. Accordingly, the DNA ladder of Stratagene is deemed to meet a limitation of each of said claims.



25. Should the prior art not anticipate the claimed invention, the selection of which band or combination of bands, and their relationship to one another is not deemed to constitute a patentable distinction over the prior art. Rather, such limitations are deemed to be the result of design choice and/or routine optimization.

26. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

> Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

27. The plurality of bands that make up each rung in the ladder of Carlson et al., and of Stratagene are deemed to have "substantially relative equal mass" as the band is shown to have "substantially equal intensities" after being separated as bands on a gel and stained. Accordingly, a limitation of claims 141-157 and 159-164 is deemed to be met by the prior art of record.

28. Claim 158 are rejected under 35 U.S.C. 103(a) as being unpatentable over either US Patent 5,316,908 (Carlson et al.) or Stratagene (1993) or Stratagene Catalog (1993) when taken in view of US Patent 5,635,365 (Ansari et al.).

29. See above for the basis of the rejection as it relates to the disclosure of both Carlson et al., and Stratagene.

30. Neither Carlson et al., nor Stratagene have been found to disclose staining the ladders with SYBR green.

31. Ansari et al., column 15, third paragraph, teaches explicitly of staining a gel with SYBR green so to enable visualization of the nucleic acid fragments separated therein.

32. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the nucleic acid ladders of either Carlson et al., or Stratagene with SYBR green as disclosed by Ansari et al., as such would have allowed the ordinary artisan with an easy, sensitive and reproducible means for detecting nucleic acids. In view of the detailed teachings in the prior art, said ordinary artisan would have had a most reasonable expectation of success.

33. For the above reasons, and in the absence of convincing evidence to the contrary, claim 158 is rejected under 35 USC 103(a) as being unpatentable over either US Patent 5,316,908 (Carlson et al.) or Stratagene (1993) or Stratagene Catalog (1993) when taken in view of US Patent 5,635,365 (Ansari et al.).

Conclusion

34. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

35. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

36. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

37. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

38. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634